REMARKS

The Claim Amendments

Claims 1-5, 7, 9-14, 16-35, 39-55, and 59 are amended to improve the form of these claims and to harmonize the claims with typical US patent practice (e.g., by replacing the referent "according to" with "of"). Claim 1 is amended to indicate that the therapeutic agent constitutes at least 40% of the composition by weight. Support for this amendment is found at, e.g., page 10, line 28, of the substitute specification previously filed in connection with this application. New claims 60-63 are directed to additional aspects and features of Applicants' invention that are supported by the specification and originally filed claims (see, e.g., original claim 8). New independent claims 64 and 66, which are directed to a solid needle-shaped pharmaceutical composition comprising a binder that consists essentially of maltitol and a needle-shaped pharmaceutical composition having a composition that is primarily comprised of maltitol, respectively, find support at, e.g., original claim 21; page 13, line 14; page 14, lines 1 and 11-14; Figure 4; and the description of Figure 4. The remaining amendments are mostly nonsubstantive in nature and directed to clarifying the claims and bringing the language therein in line with US patent practice (in certain instances *Markush*-like claim language has been removed to reinforce the independence of the recited elements in those claims). New claims 65-68 also find support in the originally filed specification. Accordingly, no new matter has been added by the claim amendments.

Claims 1-5, 7, 9-14, 16-35, 39-55, and 59-68 are pending. Claims 1, 40, 64, and 66 are the only independent claims.

The Office Action

The Office Action objected to claim 6 under 37 C.F.R. § 1.75(c) for being of allegedly improper dependent form or for failing to further limit the subject matter of claim 3. Claim 6 is hereby cancelled, obviating this objection. The cancellation of this claim in view of this

formality rejection does not constitute an amendment for reasons related to patentability. The Office Action also raises informality rejections with respect to claims 41 and 55 that are addressed by the present claim amendments. Again, these amendments are not required by any statutory requirement.

The Office Action rejected claim 11 as allegedly failing to meet the requirements of 35 U.S.C. § 112, second paragraph, inasmuch as claim 11 was dependent on a cancelled claim and used a term having no antecedent basis ("pellet"). The word "pellet" has been removed from claim 11 and the claim is now dependent on pending claim 9. These amendments, which broaden the scope of this claim (particularly with respect to the removed "pellet" element), are believed to overcome this rejection.

The Office Action maintained the prior rejections of claims 1-7, 9-14, 16-35, 39-55, and 59 based on (apparently for allegedly encompassing subject matter that would have been obvious in view of) the disclosure of International Patent Application WO 96/03978 (Roser et al. – hereinafter referred to as the "Roser '978 PCT application") and of claims 1-7, 9-14, 16-35, and 59 under 35 U.S.C. § 103(a) for allegedly encompassing subject matter that would have been obvious given the Roser '978 PCT application in view of International Patent Application WO 94/22423 (Daniel Bar-Shalom – hereinafter referred to as the "Bar-Shalom '423 PCT application"). The Office Action refers both to rejections under 35 U.S.C. 103(a) and 102(b) with respect to the Roser '978 PCT application, however a review of the prosecution history indicates that the reference to Section 102(b) with respect to the maintained claim rejections is probably an error. Nonetheless, for sake of expediting allowance of Applicants' claims, both novelty and nonobviousness will be addressed with respect to the Roser '978 PCT application and the Roser '978 PCT application and the Bar-Shalom '423 PCT application will both be addressed alone and in combination herein.

Respectfully, Applicants submit that, particularly upon entry of the foregoing claim amendments, that the pending claims are novel and nonobvious over the disclosure of the Roser '978 PCT application and/or the Bar-Shalom '423 PCT application. Accordingly, reconsideration

of these rejections is hereby solicited.

It is well established that to establish a *prima facie* obviousness rejection based upon a proposed modification to a reference, there must be a reasonable expectation of success in arriving at the claims-at-issue by the proposed modification. *See, e.g.,* MANUAL OF PATENT EXAMINING PROCEDURE ("MPEP") § 2143 (8th Ed.). In making such an assessment, the "governing standard is emphatically not whether a particular method or process leading to an invention would be 'obvious to try,' ... but whether such an experiment would have been expected to succeed." *Merck & Co. v. Danbury Pharmacal Inc.,* 694 F. Supp. 1, 29 (D. Del. 1988), *aff'd,* 873 F.2d 1418 (Fed. Cir. 1989). Moreover, "this expectation must be measured with deliberate avoidance of hindsight ..." *See id.* The expectation of success is assessed from the perspective of the person of ordinary skill in the art at the time of the invention. *See, e.g., Life Techs., Inc. v. Clontech Lab., Inc.,* 224 F.3d 1320 (Fed. Cir. 2000). That the inventors were ultimately successful in the claimed invention is irrelevant to whether one of ordinary skill in the art, at the time the invention was made, would have reasonably expected success in doing so. *See id.*

In addition to a "reasonable expectation of success," a prior art reference relied on as allegedly establishing obviousness must itself enable one of ordinary skill in the art to have practiced the claimed invention. *See e.g., Motorola, Inc. v. Interdigital Tech. Corp.,* 121 F.3d 1461, 1471 (Fed. Cir. 1997).

With respect to the subject patent application, the Office Action acknowledged that the Roser '978 PCT application does not "specifically state that the therapeutic agent should be at least 25% of the composition" and does "not explicitly disclose each of the ingredients or formulation details as claimed." See Office Action, page 10, last full paragraph. Applicants agree. Indeed, the only statement in the Roser '978 PCT application with respect to the amount of therapeutic agent that may be present is the following: "More than 20% weight percent [sic] of organic molecules can be incorporated into the HDC delivery systems." None of the examples or other description in the Roser '978 PCT application indicates that any amount of therapeutic agent above 20% could be used in a needle-shaped pharmaceutical composition while still

permitting the composition to penetrate skin or mucosa.

Claim 1 as amended is directed to a needle-shaped pharmaceutical composition comprising a homogenously-distributed therapeutic agent that constitutes at least ***40 wt.%*** of the total composition. In other words, claim 1, as amended, is directed to a composition that comprises ***at least two times*** the highest amount of therapeutic agent explicitly taught or suggested as being suitable in such a composition by even the most favorable reading of the specific teachings on the Roser '978 PCT application. Applicants respectfully submit that there would have been no reasonable expectation of success in arriving at such a composition from the vague disclosure of the Roser '978 PCT application and/or that the Roser '978 PCT application would not have enabled one of ordinary skill in the art to have made such a composition.

In support of the lack of expectation of success one of ordinary skill in the art would have had in making a composition encompassed by claim 1 at the subject application's filing date, even given the Roser '978 PCT application, Applicants submit herewith the Declaration of Thomas Buch-Rasmussen. In his Declaration, Mr. Buch-Rasmussen, a person with considerable experience in chemistry and medical device design at the time the present application was filed, states:

> Prior to the invention embodied in this [patent] application, I did not have any expectation that a pharmaceutical composition having more than about 40% of its weight made up of a therapeutic agent, distributed homogenously through the composition, would be able to penetrate skin. Indeed, the fact that such a composition can penetrate skin was surprising to me, given the common view that a very high content or increased number of therapeutic agent in a polymeric composition would render the composition unable to penetrate skin. To my recollection, there was [sic, were] no publications or other materials available at that time that taught or suggested such a pharmaceutical composition could penetrate skin (paragraph 5).
>
> * * *
>
> Even given the disclosure of the Roser '978 PCT application before the filing date [of the subject patent application], I would still have not expected that a

> pharmaceutical composition, having at least about 40% of its weight composed of a therapeutic agent homogenously distributed through the composition, would be able to penetrate skin.... I find the discovery that a composition containing at least about 40% therapeutic agent (by weight) can penetrate the skin to be surprising even over the teachings of the Roser '978 PCT application (paragraph 7).

Applicants note that in assessing obviousness "the totality of the prior art must be considered," and "proceeding contrary to accepted wisdom in the art" is to be considered strong evidence of nonobviousness. *See, e.g., In re Hedges,* 783 F.2d 1038, 228 USPQ 685 (Fed. Cir. 1986). *See also, Environmental Designs, Ltd. v. Union Oil Co. of Cal.*, 713 F.2d 693, 698 (Fed. Cir. 1983) ("Expressions of disbelief by experts constitute strong evidence of nonobviousness"); *In re Sernaker,* 702 F.2d 989, 996 (Fed. Cir. 1983) (PTO must also give weight to objective evidence of nonobviousness during patent prosecution); MPEP 2145 (preceding contrary to accepted wisdom is evidence of nonobviousness). The Buch-Rasmussen Declaration is evidence that the wisdom in the art at the filing date of the subject application was that there would be no expectation that a composition according to claim 1 could penetrate skin or mucosa. As such, Applicants respectfully submit that the Office Action's *prima facie* obviousness rejection at claim 1 is misplaced.

In view of these facts and legal principles, Applicants respectfully submit that claim 1 is nonobvious over the teachings of the Roser '978 PCT application. If an independent claim is nonobvious under 35 U.S.C. 103, then any claim depending therefrom is nonobvious. *See, e.g., In re Fine,* 837 F.2d 1071 (Fed. Cir. 1988). Accordingly, all of the claims that depend on claim 1, directly or indirectly, likewise should be deemed nonobvious over the disclosure of the Roser '978 PCT application.

Upon a full reading of the document, it is even more apparent that the Roser '978 PCT application fails to teach or suggest a composition wherein at least 40% of the composition by weight is made up of a therapeutic agent that is a peptide, polypeptide, or protein (e.g., as embodied in claim 68). Indeed, the disclosure relied on by the Office in the Roser '978 PCT application with

respect to the rejection of claim 1 relates only to "organic molecules," which are treated separately from peptides, polypeptides, and proteins in the Roser '978 PCT application (see, e.g., page 30, lines 16-28, "Such modifiers include ... organics, proteins and peptides (synthetic and natural), peptide mimetics ..." and page 30, line 32 – page 31, line 9 (providing separate definitions for "organics" and "protein")). Accordingly, even if the Roser '978 PCT application could be considered to establish the obviousness of some compositions embodied by claim 1, it is clear that those compositions would be limited to ones comprising "organic molecules," and not peptides, polypeptides, and proteins.

In seeking to overcome the above-discussed shortcomings of the Roser '978 PCT application in establishing an obviousness rejection, the Office Action relies upon the Bar-Shalom '423 PCT application. Specifically, the Office Action stated "BAR-SHALOM discloses solid pharmaceutical compositions with a shape and consistency enabling it [sic] to penetrate the skin, *consisting essentially of* the active drug substance (page 6, lines 26-24)." Respectfully, Applicants submit that the Office Action's reliance on this statement in seeking to establish a *prima facie* obviousness rejection is misplaced, particularly considering the disclosure of the Bar-Shalom '423 PCT application *as a whole* when compared to claim 1 *as a whole* (as is required – *see, e.g., In re Hedges, supra)*. In this respect, Applicants note that the Bar-Shalom '423 PCT application states:

> In an interesting embodiment of the invention the body contains the active substance or drug alone, which allows a larger amount of the active ingredient to be administered using a given size body. **The active substance will generally not be able to be moulded into a needle strong enough and with the right volume to penetrate the skin or mucosa alone.**

Page 11, lines 8-13. In view of the above passage, it is clear that the Bar-Shalom '423 PCT application ***does not*** teach or suggest a ***needle-shaped*** pharmaceutical composition that "consists essentially" of a therapeutic agent that can penetrate skin or mucosa. Applicants' representatives have found no other relevant disclosure in the Bar-Shalom '423 PCT application with respect to the therapeutic agent content of such needle-shaped compositions. Thus, the Bar-Shalom '423 PCT

application, whether taken alone or in combination with the Roser '978 PCT application, appears to do little, if anything, to address the common wisdom at the filing date of the subject patent application that a composition according to claim 1 would probably not be successful in penetrating the skin or mucosa. Nor does the Bar-Shalom '423 PCT application otherwise compensate for the shortcomings of the Roser '978 PCT application addressed above.

In addition, Applicants note that for those compositions of the Bar-Shalom '423 PCT application that include other agents or components (which apparently would be the case with respect to needle-shaped pharmaceutical composition given the above-quoted passage), the Bar-Shalom '423 PCT application teaches that such other agents should be in crystalline form (see, e.g., page 17, lines 8-10; page 22, lines 9-12; page 26, lines 23-25), in contrast to the amorphous matrix-forming binder and non-crystallization agent included in Applicants' claimed compositions. Thus, the Bar-Shalom '423 PCT application actually appears to teach away from, not towards, the aspects of Applicants' invention encompassed by claim 1.

Applicants submit that new independent claims 64 and 66 also are clearly patentable over both the Roser '978 PCT application and the Bar-Shalom '423 PCT application. Claims 64 and 66 are directed to compositions wherein either the binder consists essentially of maltitol or the composition is primarily composed of maltitol, respectively. The Roser '978 PCT application is directed to "hydrophobically derivatized carbohydrate" (HDC) compositions, which are defined as carbohydrates "where at least one hydroxyl group is substituted with a hydrophobic moiety" (page 21, lines 5-9; see also page 21, lines 31-34 (describing formula 1)). Maltitol is a *more hydrophilic* derivative of maltose. Thus, the Roser '978 PCT application actually teaches away from, not towards, the subject matter of these claims. As such, the Bar-Shalom '423 PCT application, which clearly fails to teach or suggest all of the elements of these claims, cannot be appropriately combined with the Roser '978 PCT application to address its shortcomings in teaching or suggesting all of the elements of these new claims.

In summary, Applicants respectfully submit that, when considered as a whole, the pending claims of the subject application are novel and nonobvious over the cited references.

Conclusion

The application is considered in good and proper form for allowance, and the Examiner is respectfully requested to pass this application to issue. If, in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned attorney.

Respectfully submitted,

Date: November 25, 2003

Len S. Smith, Reg. No. 43,139
Novo Nordisk Pharmaceuticals, Inc.
100 College Road West
Princeton, NJ 08540
(609) 987-5800

Use the following customer number for all correspondence regarding this application.

23650

PATENT TRADEMARK OFFICE